Among Costa Ricans, *CYP2C9*2* was also lower in the AM than in the CRM population ($P < 0.05$). Moreover, the frequency of *CYP2C9*3* in the CRM, AM and AC groups was 3.6%, 2.1% and 3.3%, respectively. *CYP2C9*6* was not detected.

Conclusion: Present data support that the *CYP2C9*2* frequency is lower in Amerindian populations than Caucasians, suggesting the importance of pharmacogenetic studies for optimizing drug dosages in different populations according to their ancestry.

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References

1. LLerena A, Dorado P, O'Kirwan F, et al. Lower frequency of *CYP2C9*2* in Mexican-Americans compared to Spaniards.. *Pharmacogenomics J.* 2004;4:403–406.
2. Dorado P, Sosa-Macias MG, Peñas-Lledó EM, et al. CYP2C9 allele frequency differences between populations of Mexican-Mestizo, Mexican-Tepehuano, and Spaniards. *Pharmacogenomics J.* 2011;11: 108–112.

PP159—C677T POLYMORPHISM OF METHYLENETETRAHYDROFOLATE REDUCTASE AND HOMOCYSTEINE CONCENTRATION IN PATIENTS WITH ESSENTIAL HYPERTENSION

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Introduction: The aim of this research was to study the prevalence of methylenetetrahydrofolate reductase (MTHFR) C677T gene polymorphismsand homocysteine concentration in male patients, European race, with mild to moderate essential hypertension.

Patients (or Materials) and Methods: The investigations were performed in 35 patients (mean age, 50.0 [5.9] years). All the patients had family history of essential hypertension. The higher prevalence of risk factors was revealed: smoking – 62.8% patients, overweight – 71.4%, dyslipidemia – 48.6%. The following defeats of targets were diagnosed: left ventricular hypertrophy – 40% patients, ultrasonic signs of carotids atherosclerosis – 82.8% patients. To identify mutations C677T of a gene MTHFR polymerase chain reaction with the subsequent restriction amplifications was used.

Results: Genotypes by MTHFR were distributed as follows: homozygotes C allele (CC genotype) was defined in 19 patients (55.9%); heterozygotes (CT genotype) in 11 patients (32.3 %); homozygotes T allele (TT genotype) in 4 patients (11.8%). Homocysteine concentration in patients with CC genotype was authentically lower than in patients with CT and TT genotype (11.34 [0.64] vs 15.33 [0.57] mkmol/L; $P < 0.001$).

Conclusion: Thus, in male patients, European race, with mild to moderate essential hypertension the prevalence of mutant allele T, determining the reduction of enzyme activity MTHFR, was 44.1%. The presence of mutant allele T was associated with a higher level of homocysteine concentration.

Disclosure of Interest: None declared.

PP161—COMPARISON OF EFFECT OF RALOXIFENE ON THE COAGULATION AND FIBRINOLYTIC SYSTEMS BETWEEN MORNING AND EVENING DOSING REGIMENS IN POST-MENOPAUSAL WOMEN WITH OSTEOPOROSIS

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Introduction: Raloxifene is a selective oestrogen receptor modulator commonly used for the treatment of postmenopausal osteoporosis. The drug is significantly associated with an increased risk of deep venous thrombosis and pulmonary embolism, probably because of its estrogenic effects on the coagulation and fibrinolytic systems. It is known that many drugs vary in potency and/or toxicity according to a dosing time. Because both the coagulation and fibrinolytic systems exhibit circadian rhythms, such adverse effects of raloxifene could be diminished by optimizing a dosing time. The aim of the present study was to investigate the effects of dosing time of raloxifene on markers of coagulation and fibrinolysis, as well as of bone metabolism.

Patients (or Materials) and Methods: Postmenopausal patients with osteoporosis were randomly allocated to 2 groups: 1 received 60-mg raloxifene once daily in the morning, whereas the other received 60-mg raloxifene in the evening, for 12 months.

Results: In both groups, the activity of coagulation Factors IX and XII significantly increased after 12 months treatment compared with baseline. The activity of coagulation Factors II and V, and levels of markers of bone metabolism (ie, bone alkaline phosphatase and tartrate-resistant acid phosphatase 5b) decreased in both groups. The changes in these markers did not differ between the 2 groups. In contrast, the plasma concentration of plasminogen activator inhibitor-1 increased in the patients with the morning dose but not in the patients with the evening dose.

Conclusion: Because the elevated concentration of plasminogen activator inhibitor-1 is shown to be associated with the risk of venous thromboembolism, these data suggest that the evening dose of raloxifene is relatively safe dosage regimen.

Disclosure of Interest: None declared.

PP162—THOROUGH QT STUDY WITH PONESIMOD, A SELECTIVE S1P1 RECEPTOR MODULATOR

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Introduction: Ponesimod is a selective sphingosine-1 phosphate (S1P1) receptor modulator currently in clinical development for multiple sclerosis and plaque psoriasis. Drug-induced prolongation of the QT interval can lead to torsades de pointes and sudden cardiac death. The aim of this study was to assess whether ponesimod has a negative QT/QTc effect as per ICH E14 guidance in a thorough QT/QTc study.

Patients (or Materials) and Methods: This was a single-center, double-blind, placebo- and positive-controlled (400-mg moxifloxacin), parallel group with nested crossover, up-titration study in 116 healthy male and female subjects (58 subjects on ponesimod and 58 subjects on moxifloxacin/placebo). All subjects received placebo for ponesimod on day –1. In treatment group A, ponesimod was administered orally once daily for 22 days (10 mg on days 2–4, 20 mg on days 5–7, 40 mg on days 8–12, 60 mg on days 13–15, 80 mg on days 16–18, and 100 mg on days 19–23). In addition, subjects received placebo